

Amendments to the Specification:

Following the abstract, please insert the attached Sequence Listing with subsequent page numbering thereafter.

Please replace the paragraph at page 4, lines 4-7 with the following amended paragraph:

The invention also provides a pharmaceutical composition useful for inducing an immune response to Jaagsiekte sheep retrovirus (JSRV) in ~~an~~ a subject. The composition includes an immunogenically effective amount of a JSRV or JSRV polypeptide in a pharmaceutically acceptable carrier.

Please replace the paragraph at page 4, lines 8-13 with the following amended paragraph:

In another embodiment, a method of inducing an immune response to a JSRV or JSRV polypeptide in a subject is provided. The method includes immunizing an animal with ~~the composition~~ a pharmaceutical composition useful for inducing an immune response to Jaagsiekte sheep retrovirus (JSRV) in an subject. The composition includes an immunogenically effective amount of a JSRV or JSRV polypeptide in a pharmaceutically acceptable carrier.

Please replace the paragraph at page 6, lines 6-14 with the following amended paragraph:

FIG. 5 shows the alignment of the deduced amino acid sequence of *gag* of type D retrovirus of sheep. Alignment is shown of the exogenous JSRV₂₁ (AF105220) (SEQ ID NO:9), JSRV-SA (M80216) (SEQ ID NO:10), ENTV (Y16627) (SEQ ID NO:11) and the endogenous en5F16 (SEQ ID NO:12) and en56A1 (SEQ ID NO:13) that maintain an open reading frame along the whole *gag*. Dots refer to identical sequences while dashes indicate lack of sequence. Underlined are the variable region A and B (VRA and VRB). Note the proline rich region present in the VRA of the exogenous JSRVs and ENTV that is instead absent in the endogenous

loci. In VRB, ENTV is more similar to JSRV than *enJSRVs*. Indicated is the putative major capsid region (CA) and the *HpaI* site used to generate exogenous-endogenous chimeras.

Please replace the paragraph at page 6, lines 16-22 with the following amended paragraph:

FIG. 6 shows the alignment of the deduced amino acid sequence of *env* of type D endogenous retroviruses of sheep. Alignment is shown of the exogenous JSRV₂₁ (AF105220) (SEQ ID NO:14), JSRV-SA (M80216) (SEQ ID NO:15), ENTV (Y16627) (SEQ ID NO:16) and the endogenous enJS5F16 (SEQ ID NO:17) and enJS56A1 (SEQ ID NO:18) that maintain an open reading frame along the whole *env*. Dots refer to identical sequences while dashes indicate lack of sequence. The boundaries between the surface (SU) and transmembrane (TM) are indicated. The variable region C (VRC) is underlined. Note the polymorphism between all the sequences in VRC.

Please replace the paragraph at page 6, lines 30-34 with the following amended paragraph:

FIG. 8 shows the alignment of the nucleotide sequence of the untranslated *gag* region of type-D retroviruses of sheep. Alignment is shown of the exogenous JSRV₂₁ (AF105220) (SEQ ID NO:19), JSRV-SA (M80216) (SEQ ID NO:20), ENTV (Y16627) (SEQ ID NO:21) and the endogenous enJS5F16 (SEQ ID NO:22), enJS59A1 (SEQ ID NO:23) and enJS56A1 (SEQ ID NO:24). The primer binding site (PBS) is underlined.

Please insert the following paragraph at page 7 prior to the "Detailed Description of the Invention":

Applicants made the following biological deposit under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure:

Definition: Ovine pulmonary adenocarcinoma virus, complete genome
Accession No.: AF105220
Date of Deposit: July 25, 2001

Please replace the paragraph at page 11, line 31 through page 12, line 4 with the following amended paragraph:

Sequence analysis showed that a JSRV₂₁, isolated as described below, possesses the hallmarks of integrated retroviral proviruses, such as the presence of a CA-TG dinucleotide pair present at the termini of the upstream and downstream viral LTRs, the loss of 2 nucleotides (nt) from the termini of the LTRs during integration, and an apparent duplication of 6 nt of cellular flanking sequences (TGTGTC (~~SEQ ID NO: 8~~)) at the integration site. The flanking cellular sequences in the JSRV₂₁ clone were 393 and 1,006 bp long and did not align with known cellular sequences (including proto-oncogenes).

Please replace the paragraph at page 23, line 30 through page 24, line 11 with the following amended paragraph:

In one embodiment, the invention provides an isolated polynucleotide sequence corresponding to the isolated genome of JSRV. Polynucleotide sequences of the invention include DNA, cDNA and RNA sequences. It is understood that all polynucleotides encoding all or a portion of a JSRV genome are included herein. Such polynucleotides include naturally occurring, synthetic, and intentionally manipulated polynucleotides. For example, a JSRV polynucleotide of the invention includes the JSRV sequence having accession number AF105220 (SEQ ID NO:8). In addition, a polynucleotide of the invention includes a fragment of the sequence having accession number AF105220 as well as sequences subjected to site-directed mutagenesis. The polynucleotides of the invention include sequences that are degenerate as a result of the genetic code. There are 20 natural amino acids, most of which are specified by more than one codon.

Therefore, all degenerate nucleotide sequences are included in the invention so long as a protein encoded by a JSRV genome is functionally unchanged.

Please replace the paragraph at page 26, line 28 through page 27, line 26 with the following amended paragraph:

Other algorithms for determining homology or identity include, for example, in addition to a BLAST program (Basic Local Alignment Search Tool at the National Center for Biological Information), ALIGN, AMAS (Analysis of Multiply Aligned Sequences), AMPS (Protein Multiple Sequence Alignment), ASSET (Aligned Segment Statistical Evaluation Tool), BANDS, BESTSCOR, BIOSCAN (Biological Sequence Comparative Analysis Node), BLIMPS (BLocks IMProved Searcher), FASTA, Intervals & Points, BMB, CLUSTAL V, CLUSTAL W, CONSENSUS, LCONSENSUS, WCONSENSUS, Smith-Waterman algorithm, DARWIN, Las Vegas algorithm, FNAT (Forced Nucleotide Alignment Tool), Framealign, Framesearch, DYNAMIC, FILTER, FSAP (Fristensky Sequence Analysis Package), GAP (Global Alignment Program), GENAL, GIBBS, GenQuest, ISSC (Sensitive Sequence Comparison), LALIGN (Local Sequence Alignment), LCP (Local Content Program), MACAW (Multiple Alignment Construction & Analysis Workbench), MAP (Multiple Alignment Program), MBLKP, MBLKN, PIMA (Pattern-Induced Multi-sequence Alignment), SAGA (Sequence Alignment by Genetic Algorithm) and WHAT-IF. Such alignment programs can also be used to screen genome databases to identify polynucleotide sequences having substantially identical sequences. A number of genome databases are available, for example, a substantial portion of the human genome is available as part of the Human Genome Sequencing Project (J. Roach, http://weber.u.Washington.edu/~roach/human_genome_progress2.html) (Gibbs, 1995). At least twenty-one other genomes have already been sequenced, including, for example, *M. genitalium* (Fraser *et al.*, 1995), *M. jannaschii* (Bult *et al.*, 1996), *H. influenzae* (Fleischmann *et al.*, 1995), *E. coli* (Blattner *et al.*, 1997), and yeast (*S. cerevisiae*) (Mewes *et al.*, 1997), and *D. melanogaster* (Adams *et al.*, 2000). Significant progress has also been made in sequencing the genomes of model

organism, such as mouse, *C. elegans*, *Arabidopsis sp.* and *D. melanogaster*. Several databases containing genomic information annotated with some functional information are maintained by different organization, and are accessible via the internet, for example, <http://www.tigr.org/tdb>; <http://www.genetics.wisc.edu>; <http://genome-www.stanford.edu/~ball>; <http://hiv-web.lanl.gov>; <http://www.ncbi.nlm.nih.gov>; <http://www.ebi.ac.uk>; <http://Pasteur.fr/other/biology>; and <http://www.genome.wi.mit.edu> <http://www.genome.wi.mit.edu>.

Please replace the paragraph at page 66, lines 5-23 with the following amended paragraph:

Plasmid pCMV2JS₂₁ was generated by replacing the U3 region in the upstream LTR of pJSRV₂₁ with the human cytomegalovirus (CMV) immediate-early promoter by methods known in the art (Sambrook, J., E. F. Fritsch, and T. Maniatis. 1989. Molecular cloning: a laboratory manual, 2nd ed. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.). The CMV promoter was obtained by PCR amplification from the pCDNA3 plasmid (Invitrogen) with primers CMVNotIf (AAAGGGTTGCGGCCGCCGATGTAC GGGCCAGATATAC (SEQ ID NO:[____]1)) and CMV-r2 (CAGAGAGCTCTGC TTATATAGACCTCCCAC (SEQ ID NO:[____]2)) and the Pfu Turbo polymerase (Stratagene) under PCR conditions as suggested by the manufacturer. The resulting PCR product was cut with *NotI* and then ligated to an amplified portion of JSRV₂₁ spanning position 13 in the U3 to +618 in gag. This portion of JSRV₂₁, which includes R, U5, and the beginning of gag, was amplified by PCR with primers JS21-R (GCATTGTAATAAAGCAGAGTATCAGCC (SEQ ID NO:[____]3)) and JS21663-r (GGAACCAAGGGCAAACCTCCTCAATAAATGAA (SEQ ID NO:[____]4)) and the Pfu Turbo polymerase as above. The ligation reaction mixture was reamplified by PCR with primers CMVNotIf and JS21663-r, and the resulting product was digested with *NotI* and *PacI* and inserted into *NotI*-*PacI*-digested JSRV₂₁ to give pCMV2JS₂₁ (FIG. 2).

Please replace the paragraph at page 66, lines 25-31 with the following amended paragraph:

Sequence analysis showed that JSRV₂₁ possesses the hallmarks of integrated retroviral proviruses, such as the presence of a CA-TG dinucleotide pair present at the termini of the upstream and downstream viral LTRs, the loss of 2 nucleotides (nt) from the termini of the LTRs during integration, and an apparent duplication of 6 nt of cellular flanking sequences (TGTGTC (SEQ ID NO:)) at the integration site. The flanking cellular sequences in the JSRV21 clone were 393 and 1,006 bp long and did not align with known cellular sequences (including proto-oncogenes).

Please replace the paragraph at page 76, lines 1-9 with the following amended paragraph:

Oligonucleotides. For the electrophoretic mobility shift assays (EMSA) the following double stranded oligonucleotide probe were used: JS₂₁wt(-267/-247) (TGCGGGGGACGAC CCGTGAA (SEQ ID NO:[]]5)) and JS₂₁mt(-267/-247) (TGCGG**TTT**ACGACCCGTGAA (SEQ ID NO:[]]6); mutated nucleotides are shown in bold). JS₂₁wt(-266/-247) corresponds to position -266 to -247 of the U3 of JSRV₂₁ and includes an NF- κ B-like binding site (underlined). JS₂₁mt(-266/-247) has three nucleotides changes (in bold) with respect to JS₂₁wt(-267/-247) to alter the NF- κ B-like site. Oligonucleotide probes for the consensus sequence of NF- κ B were purchased from Geneka as positive controls.

Please replace the paragraph at page 86, lines 24-32 with the following amended paragraph:

An NF κ B binding site is important for expression of the JSRV LTR. Approximately one-half of the enhancer activity of the JSRV LTR in MLE-15 and mtCC1-2 cells could be attributed to elements in the distal region (-239 to -266). This region contains an NF κ B-like binding side with one mismatch (5'-GGGACGACC-3' (SEQ ID NO:)) from the canonical NF κ B consensus binding sequence (5'-GGGPuNNPyPyCC-3' (SEQ ID NO:[]]7). To test if this binding side was important for the enhancer activity in the distal region of the JSRV LTR,

a version of pJS21-luc was generated in which the NF κ B-like site was mutated (pNF κ Bm-luc). The activity of pNF κ Bm-luc was compared to pJS21-luc in various cell lines and the relative activity of pJS21-luc was set as 100.

Please replace the paragraph at page 97, lines 25-29 with the following amended paragraph:

From the constructed trees (Fig. [[____]]9a to c), the endogenous loci can be divided in at least two phylogenetic groups: *enJSRV-A*, *enJSRV-B*. Another one or two groups might arise (e.g., proviruses where the sequences locus 5 and 6 were derived might form a group separate from *enJSRV-A*) but complete proviral sequences need to be obtained in order to fully classify these elements.